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DR. WILLIAM J. KERR, San Francisco, *Editor*

DR. JOHN J. SAMPSON, San Francisco, *Associate Editor*

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THE THERAPEUTIC ACTION OF DIGITALIS: MODE OF ADMINISTRATION

The therapeutic action of digitalis is directed toward the improvement or the preservation of circulatory function, not to the cure or prevention of disease. In appropriate cases the drug is administered with the object of improving the circulation, whatever disease may be the ultimate cause of impairment. It is used also to prevent circulatory insufficiency in certain circumstances under which impairment might be expected to result.

It must be noted that no sharp division between the above two classes of cases can be made. In the presence of conditions which lead to diminution of circulatory function it may be impossible to fix precisely the point at which impairment begins. It appears that failure to keep this fact in mind has sometimes confused the problem of correct digitalis therapy.

RESULTS OF ADMINISTRATION: It is well known that in some cases which present proper indications for the employment of digitalis, little benefit follows correct administration. The effects of disease may be so great as to destroy any capacity for functional improvement by the drug. In appropriate cases less severely affected, however, certain clinical evidences of favorable effect have long been recognized. In general these beneficial results are manifested as follows:

1. In cases of congestive heart failure, the signs and symptoms of impaired cardiac efficiency diminish or disappear. The circulation improves. Dyspnea, peripheral edema and evidences of visceral congestion are lessened. Output of urine increases. The patient feels better. If tachycardia has been in evidence the rate diminishes. In normal rhythm cases, this diminution of ventricular rate is not a direct effect of digitalis but occurs subsequently to the improvement produced by it; it represents a reflex adjustment to circulatory improvement. In auricular fibrillation cases of congestive failure, the explanation of the slowing is open to question. The matter will receive brief comment under "Pharmacologic Effects."

2. In certain cases in which conditions are present which commonly cause failure, impairment of cardiac efficiency is prevented or postponed. This group includes not only cases in which congestive failure has been present, but also other cases presenting evidences of disease processes which tend toward that result; e.g., conditions which involve strain relating especially either to the left or to the right ventricle. It is probable that in many if not in most instances of so-called "potential" heart failure, some measure of circulatory insufficiency already has occurred, even though the fact may not readily be demonstrated. Such cases properly should be designated as "early" rather than as "potential" failure. It is evident that the value of digitalis in obviating congestive heart failure is not susceptible of proof in some single instance. Upon consideration of its employment in large numbers of cases, however, it is difficult to avoid the conclusion that the drug is of great value in properly selected instances.

3. In cases of auricular fibrillation without congestive failure there is difference of opinion as to the slowing effect of digitalis in dosage comparable to that which induces reduction of rate in heart failure cases. It is agreed that in many such instances no slowing is produced. This applies particularly to those cases in which the arrhythmia results from some toxic agent, and probably also to cases of nervous origin. Among the precipitating causes of fibrillation the chief remaining factor appears to be auricular distention such as results from congestive failure. Fibrillation has been called "an important evidence of the existence of heart failure." Not infrequently it may be one of the earliest evidences. The common notion regarding the ability of digitalis to reduce ventricular rate in non-heart-failure cases of fibrillation thus appears to rest largely on incorrect classification, such cases actually being instances of early (unrecognized) congestive failure, the fibrillation having been produced by the associated distention of the auricle.

PHARMACOLOGIC EFFECTS: The pharmacologic effects responsible for the favorable results of

SCIENTIFIC SESSIONS

The Thirteenth Scientific Sessions of the American Heart Association will be held in the Viking Room, Chalfonte-Haddon Hall, Atlantic City, June 7 and 8, 1937. The program of the Section for the Study of the Peripheral Circulation will be given on Monday, June 7, and the general cardiac program on Tuesday, June 8.

The American Heart Association joins the American Medical Association in a heart symposium in Atlantic City, June 7-11. Don't fail to visit our exhibit booths at the Auditorium!

digitalis therapy relate principally, if not exclusively, to the action of the drug upon the heart, most authorities believing that constriction, whether of the arterioles or of the hepatic vein, is not a consequential factor in the improvement of the circulation. More recent investigations regarding the effects on heart muscle, furthermore, refer the beneficial effects to the muscular action:

(a) The relative oxygen requirement is lessened; mechanical efficiency is raised.

(b) The size of the ventricle is decreased; in cases of dilatation it becomes more nearly optimal.

(c) In the normal heart, ventricular output is lessened, an effect due apparently to the decrease in heart size, but authorities are not in entire agreement regarding the effect on the amount of blood discharged with systole in cases of congestive heart failure. Most investigators find that the reduced output characteristic of heart failure is raised temporarily, if not more persistently. Upon this basis they explain the relief of venous stasis by digitalis in failure cases.

(d) In cases of congestive failure, the facility of ventricular response to auricular stimuli is diminished. This is shown by the reduction of ventricular rate in those failure cases that also exhibit auricular fibrillation. Prior to demonstration of the favorable action of digitalis directly on the muscle in congestive failure, this slowing was explained as due to a special action of the drug upon the a-v tissues. Now, however, there is much evidence in favor of the view that it results largely from the lessening of ventricular irritability which accompanies the muscular effect that obtains regularly in cases of heart failure.

Whether there is some favorable action of the drug limited particularly to the a-v tissues, appears questionable. In view, however, of authoritative opinion long entertained in favor of a special conduction effect, newer evidence may yet hardly permit such a conception to be dismissed. The problem obviously is linked to the question of slowing in non-failure cases of fibrillation.

MODE OF ADMINISTRATION: On the basis of present knowledge the whole leaf in tablets, pills, or capsules is to be preferred to some special product. The tincture usually is satisfactory. Only in cases in which the patient cannot take the drug by mouth, or is unable to retain it, should resort be had to other avenues of administration. Under such circumstances it may be given per rectum, intravenously or, if necessary, intramuscularly. A suspension of the powdered leaf or a dilute tincture may be used for rectal administration. Various special products are available for intravenous use.

The dose by which a certain effect is produced is called the *effective* dose; that by which a particular level of effect is maintained, the *maintenance* dose.

Variation in the degree of heart failure may make it desirable to produce or to maintain digitalis effect at different levels in different patients, or, under different circumstances, in the same patient. In some instances, but not in most, the highest possible effect, just short of the toxic level, is indicated. Whether high or low in extent it is obvious that the optimum level is that degree of effect at which the signs of circulatory insufficiency are least in evidence. The *optimum* dose is to be distinguished from the highest tolerated dose. It is the smallest dose under which optimum effect is produced or maintained. In severe cases it may approach toxic dosage, but in instances of less extreme heart disease or heart failure there is a considerable margin between the optimum level of effect and the highest level that can be reached and maintained.

Optimum dosage in an individual case can be determined only by observation of effects produced in that case by various amounts. It is rarely necessary to reach maximum effect with great rapidity. Undue haste in administration involves the danger of serious intoxication without affording commensurate advantage. For in administering more deliberately successive amounts of the total dosage (up to the optimum quantity), increasing benefit accrues to the heart, and the effect of the successive fractions can be gauged. Additional effect obviously should not be sought if (1) satisfactory effect is attained or if (2) toxic action is induced. In most cases in which digitalis has not recently been administered the amount so ordered will be from 1.0 gram to 2.0 grams.

In the induction of digitalis effect by such a fractional method of administration, and particularly in the maintenance of it, account must be taken of the rate of elimination. More recent data clearly show that elimination is proportioned to the amount present in the body. In other words, to maintain a high level of effect the daily ration must be an amount considerably larger than that with which a low level is maintained. This is equivalent to saying that among various patients there is great variation in the correct maintenance dose. In an individual case also it is evident that as the need for a different level of effect may arise, so the necessity for a different maintenance dose may ensue. Whether the optimum amount to be administered daily be as little as 0.03 gram or as much as 0.3 gram, it is only by the effect produced that the correct maintenance dose can be determined.

Drew Luten, M.D.
St. Louis, Missouri

ANNOUNCEMENT!

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